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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,226	03/09/2004	Michael Collins	PC19103B	4162

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AGOURON PHARMACEUTICALS, INC.
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EXAMINER	
AULAKH, CHARANJIT	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,226	COLLINS ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *76-78* is/are allowed.

6)☒ Claim(s) *52-75 and 79-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. According to a preliminary amendment filed on March 9, 2004, the applicants have canceled claims 1-51 and furthermore, have added new claims 52-103.

2. Claims 52-103 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 80-101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of prior art and the breadth of claims.

The instant compounds are protein kinase inhibitors as demonstrated by inhibiting receptor autophosphorylation induced by growth factors such as VEGF or FGF (see table 1). However, there is no teaching in the specification or prior art that VEGF and FGF are involved in the etiology of every known proliferative disorder, every known kidney disease, angiogenesis, pancreatitis and blastocyte implantation. There are no working examples present showing efficacy of instant compounds in known animal models of every known proliferative disorder, every known kidney disease, angiogenesis, pancreatitis and blastocyte implantation. The instant compounds of formula I encompasses several hundreds of thousands of compounds based on the values of variables R11, Y, Z, R14, R15, R16 and R17 and therefore, in absence of such teachings, guidance or working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of every known proliferative disorder, every known kidney disease, angiogenesis, pancreatitis and blastocyte implantation and hence their utility for treating these disease conditions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 80-101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 80-85 and 91-96, the term ---hyperproliferative disorder---- is indefinite since specific disorders which are supported by the instant specificationare not defined.

In claims 86 and 97, the term ---kidney disease---- is indefinite since specific diseases which are supported by the instant specification are not defined.

In claims 87 and 98, the term ---prevention---- is indefinite since the degree of prevention (20%, 40%, 60%, 80% or 100%) is not defined.

In claims 88-90 and 99-101, the term ---disease related to vasculogenesis or angiogenesis---- is indefinite since specific diseases are not defined and furthermore, what is their relationship to vasculogenesis or angiogenesis?

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 52-71 and 80-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Munchhof (WO 99/24440, cited on applicants form 1449).

Munchhof discloses Thienopyridine derivatives for treating hyperproliferative disorders. The closely related exemplified compounds (see examples 48-60) disclosed by Munchhof differ from the instant compounds (when z is N and Y is NH in the instant compounds) by lacking –CONH-R14 substitution on the indole ring. However, indole ring (variable R2 in the compounds of Munchhof), which are specifically preffered compounds (see page 4, lines 9-10) may be optionally substituted with R5 group such as –C(O)NR6R7 (see page2, lines 30-31). Therefore, it would have been obvious to one skilled in the art to prepare the instant compounds without losing their utility for treating hyperproliferative disorders since substitution of indole ring is not critical for the intended utility as taught by Munchhof unless applicants provide evidence of unexpected results such as superior activity of the instant compounds with this specific substitution on the indole ring as compared to prior art compounds with unsubstituted indole ring.

10. Claims 52-75 and 79-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx (WO 03/000194, cited on applicants form 1449).

Marx discloses Thienopyridine derivatives for treating hyperproliferative disorders. The closely related exemplified compounds (see examples 1-11 and 14-16) disclosed by Marx differ from the instant compounds (when z is N and Y is O in the instant compounds) by lacking –CONH-R14 substitution on the indole ring. However, indole ring (variable R1 in the compounds of Marx), which are specifically preffered compounds (see page 6, lines 29-30) may be optionally substituted with R5 group such as –C(O)NR6R7 (see page2, lines 29-30). Therefore, it would have been obvious

to one skilled in the art to prepare the instant compounds without losing their utility for treating hyperproliferative disorders since substitution of indole ring is not critical for the intended utility as taught by Marx unless applicants provide evidence of unexpected results such as superior activity of the instant compounds with this specific substitution on the indole ring as compared to prior art compounds with unsubstituted indole ring.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625